

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re patent application of

Muhlradt

Confirmation No. 5050

Serial No. 10/521,013

Group Art Unit 1654

Filed September 13, 2005

Examiner Ha

For BISACYLOXYPROPYLCYSTEINE CONJUGATES AND THE USE  
THEREOF

Commissioner for Patents  
PO Box 1450  
Alexandria, Virginia 22313-1450

RESPONSE TO RESTRICTION REQUIREMENT

Sir:

In response to the Restriction Requirement mailed November 13, 2006, the applicant elects, with traverse, the following species:

The elected species is a bisacyloxypropylcysteine conjugate wherein the residues R1 and R2 may be identical or different and are C8-C22 alkyl, alkenyl or alkynyl groups as identified in claim 2, the residue is a polyethylene glycol residue, Y is oxygen, and X is OR where R=hydrogen.

An exemplary compound within the elected species is the bisacyloxypropylcysteine conjugate identified as S-[2,3-bis(acyloxy)-(2Sor2R)-propyl][L-cysteinylcarboxypolyethyleneglycol which is specifically mentioned in claims 5 and 6, respectively.

Claims 1-10 read on the elected species.

It is noted that the application is a national stage filing based on PCT application PCT/EP2003/007892. At the international stage, all claims were considered as noted from the International Search Report. Thus, restriction of the invention to a particular species after all claims have been considered at the international stage appears to improper. Further, there should not be an undue

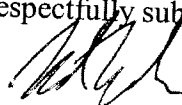
burden on the Examiner as claims have already been identified as being allowable in Europe. For the Examiner's convenience, I have attached the claims deemed to be allowable in Europe. The elected species is within the claims deemed to be allowable in Europe.

Reconsideration of the restriction requirement, and examination of the claims in view of this response at an early date, is requested.

Should the Examiner find the application to be other than in condition for allowance, the Examiner is requested to contact the undersigned at the local telephone number listed below to discuss any other changes deemed necessary in a telephonic or personal interview.

A provisional petition is hereby made for any extension of time necessary for the continued pendency during the life of this application. Please charge any fees for such provisional petition and any deficiencies in fees and credit any overpayment of fees to Attorney's Deposit Account No. 50-2041.

Respectfully submitted,



Michael E. Whitham  
Reg. No. 32,635

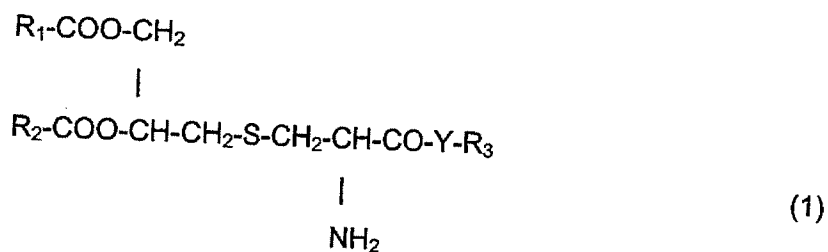
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## claims 1-10

1. A bisacyloxypropylcysteine conjugate according to formula 1,

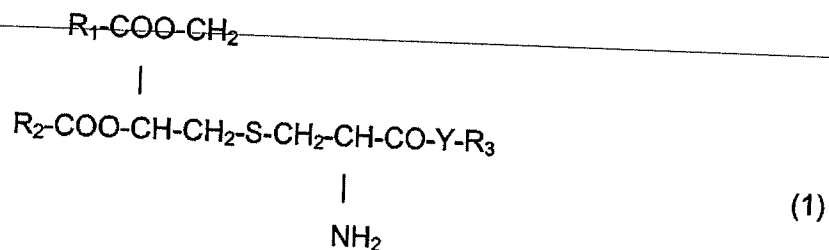


where R1 and R2 can be identical or different and are fatty acid residues which are bonded by way of the carboxyl group,

Y = -NH-, -O-, -S- or -OCO-,

R3 is a water soluble and physiologically tolerated, covalently bonded polymer,

and where the polymeric substituent R3 is substituted once, twice or several times by



2. A bisacyloxypropylcysteine conjugate as claimed in claim 1, characterized in that the polymer is selected from the group consisting of covalently bonded polyethylene glycol  
 $-(\text{CH}_2\text{-CH}_2\text{-O})_m\text{-CH}_2\text{-CH}_2\text{-X}$ ,  
 where X = OR, N(R)<sub>2</sub>, SR, COOR and  
 R = H, benzyl-, C<sub>1-6</sub> alkyl, where several substituents R can be identical or different  
 a polyoxyethylene-polyoxypropylene copolymer, a dextran, a sugar, a polyvinylpyrrolidone, an alginate, a pectin or a collagen.

3. A bisacyloxypropylcysteine conjugate according to claim 2, characterized in that a polymer is a covalently bonded polyethylene glycol  $-(CH_2-CH_2-O)_m-CH_2-CH_2-X$ , with  $X = OR, N(R)_2, SR, COOR$  and  $R = H, \text{benzyl-}, C_{1-6} \text{ alkyl}$ , where several substituents can be identical or different.
4. A bisacyloxypropylcysteine conjugate according to any one of claims 1 to 3, characterized in that the residues  $R_1, R_2$  which can be identical or different, are  $C_{7-25}$ -, preferably  $C_{8-22}$ -alkyl, -alkenyl or -alkynyl groups and the unsaturated positions are preferably in the cis-configuration, with the alkyl, alkenyl and alkynyl radicals being branched or unbranched, cyclic or cycloalkyl-substituted substituents.
5. A bisacyloxypropylcysteine conjugate according to any one of claims 1 to 4, characterized in that the molecular weight of a water soluble polymer substituent is selected such that it amounts to from 100 to 30 000 Daltons per conjugate molecule.
- ~~6. A bisacyloxypropylcysteine conjugate according to any one of claims 1 to 5, characterized in that the polyethylene glycol of the substituent  $R_3$  has a chain length  $m$  of from 5 to 700, preferably of 100 to 500.~~
7. A bisacyloxypropylcysteine conjugate according to any one of claims 1 to 6, characterized in, that the compound is a S-[2,3-bis(acyloxy)-(2S)-propyl]-L-cysteinyl-carboxy-polyethylene glycol, preferably S-[2,3-bis(palmitoyloxy)-(2S)-propyl]-L-cysteinyl-carboxy-polyethylene glycol.
8. A bisacyloxypropylcysteine conjugate according to any one of claims 1 to 7, characterized in, that the compound is a S-[2,3-bis(acyloxy)-(2R)-propyl]-L-cysteinyl-carboxy-polyethylene glycol, preferably S-[2,3-bis(palmitoyloxy)-(2R)-propyl]-L-cysteinyl-carboxy-polyethylene glycol.

9. A pharmaceutical composition, comprising a bisacyloxypropylcysteine conjugate as claimed in any one of claims 1 to 8.
  10. A pharmaceutical composition as claimed in claim 9, characterized in that it comprises pharmaceutical additives or auxiliary substances and, preferably a pharmaceutically tolerated excipient.
  11. A pharmaceutical composition according to claim 9 or 10 in the form of a formulation which is suitable for injection, for inhalation or for intranasal or topical administration.
  12. Use of the bisacyloxypropylcysteine conjugate according to any one claims 1 to 8 or a pharmaceutical composition according to claims 9, 10 or 11, for the preparation of a medicament for the treatment of tumors, for preventing or treating septic shock, for wound healing or for use as an adjuvant for vaccines.
  13. Vaccines, characterized in that it comprises a bisacyloxypropylcysteine conjugate according to any one of claims 1 to 8.
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